PTO-850-(Rev. 09-10-96)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
McDonald	08/330517	10/27/94	5,593,666	1/14/97

If application has been patented, have maintenance fees been paid? ___Yes ___No X Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/291376	8/16/94	NONE	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 1-12, 14-18, 20-27

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 13, 19

UNPATENTABLE PENDING CLAIMS: —

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Boosel man	08/252628	5/31/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/221768	3/31/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 37, 38, 40-46

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

EYI

AUG 4 1998

RECEIVED IN BOX INTERFERENCE

Instructions

1. For every patent involved in the interference, check if the maintenance fees have been paid by using the patent number with PALM screen 2970. If fees are due and they have not been paid, the interference cannot be declared since it would involve an expired patent (35 USC 135(a); 37 CFR 1.606).
2. For each party, identify the patentable (or patented) and unpatentable (pending) claims which correspond to the count (37 CFR 1.601(f), (n); 1.609(b)(2)).
3. For each party, identify the patentable (or patented) and unpatentable (pending) claims which do not correspond to the count (37 CFR 1.609(b)(3)).
4. Forward all files including those the benefit of which is being accorded.
5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate typewritten sheet(s).

6. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention as the count (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention from the count (37 CFR 1.609(b)(3).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE 12/19/97	GROUP DIRECTOR SIGNATURE (if required)		

**The application number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

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INTERFERENCE INITIAL MEMORANDUM

Count # 1

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This interference involves ____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Bartley	08/481265	6/24/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
PCT	US95/03776	3/30/95	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
86	84, 85, 87-92

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Bartley	08/413802	3/30/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/347780	11/30/94	—	—
US	08/321488	10/12/94	—	—
US	08/252628	5/31/94	—	I-Y1 —
US	08/221768	3/31/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
144-151	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

AUG 4 1998

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DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary C Lee		

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INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
EATON	08/196689	2/15/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/185607	1/21/94		
US	08/176553	1/3/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 11-13, 16-20, 28-38

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/249376	5/25/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/223263	4/14/94	—	—
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	I-Y1 —
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 26-31, 38-46

UNPATENTABLE PENDING CLAIMS: —

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The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

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Instructions

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DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary Clem		

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INTERFERENCE INITIAL MEMORANDUM

Count #_____

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves _____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/348658	12/2/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
13, 15, 16	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/422020	4/13/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/223263	4/4/94		
US	08/196689	2/15/94		
US	08/185607	1/21/94		
US	08/176553	1/3/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
20-23, 32-42	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

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AUG 4 1998

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Instructions

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DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary C Lee		

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Count # 1

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PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/431378	4/27/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 16-21, 28

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/433103	5/3/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/374540	1/19/95	—	—
PCT	US94/14553	12/28/94	—	—
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	—
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

AUG 4 1998

RECEIVED IN BOX INTERFERENCE

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 22-26, 28-33, 40-42

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

3. For each party, identify the patentable (or patented) and unpatentable (pending) claims which do not correspond to the count (37 CFR 1.609(b)(3)).
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DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Jonathan Hoxton	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

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PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/223263	4/4/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 1, 4, 7, 9, 28, 30-37, 40

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/348657	12/2/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 1, 2, 19

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

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AUG 4 1998

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Instructions

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2. For each party, identify the patentable (or patented) and unpatentable (pending) claims which correspond to the count (37 CFR 1.601(f), (n); 1.609(b)(2)).
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DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary Chan		

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PTO-850-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM Count # 1

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PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/425095	4/18/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/249376	5/25/94		
US	08/223263	4/4/94		
US	08/196689	2/15/94		
US	08/185607	1/21/94		
US	08/196553	1/3/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 1, 34, 38-40, 44-46 | UNPATENTABLE CLAIMS:

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: | UNPATENTABLE CLAIMS:

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/429365	4/26/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/348658	12/2/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	1-4

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 1, 2, 4, 24, 26, 27 | UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — | UNPATENTABLE CLAIMS: —

AUG 4 1998

RECEIVED IN BOX INTERFERENCE

Instructions

1. For every patent involved in the interference, check if the fees have been paid by using the **patent number** with the PALM screen CR06.
   If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC 135(a); 37 CFR 1.606).
2. For each party, separately identify the patentable and unpatentable claims which correspond to the count. (37 CFR 1.601 (f), 1.601 (n), 1.609(b)(2)).
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12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

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Count # 1

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This interference involves ____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/430018	4/27/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 1, 3-5, 24, 26-31

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/422194	4/13/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/223263	4/4/94	—	—
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: 1, 28, 32-42

UNPATENTABLE PENDING CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS: —

UNPATENTABLE PENDING CLAIMS: —

Instructions

1. For every patent involved in the interference, check if the maintenance fees have been paid by using the patent number with PALM screen 2970. If fees are due and they have not been paid, the interference cannot be declared since it would involve an expired patent (35 USC 135(a); 37 CFR 1.606).
2. For each party, identify the patentable (or patented) and unpatentable (pending) claims which correspond to the count (37 CFR 1.601(f), (n); 1.609(b)(2)).
3. For each party, identify the patentable (or patented) and unpatentable (pending) claims which do not correspond to the count (37 CFR 1.609(b)(3)).
4. Forward all files including those the benefit of which is being accorded.
5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate typewritten sheet(s).

6. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention as the count (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention from the count (37 CFR 1.609(b)(3).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The application number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 09-10-96)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves _____ parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/423194	4/18/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	—
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
1, 2, 6, 17, 38-45	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/425016	4/18/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of: COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	—
US	08/196689	2/15/94	—	FYI
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
1, 2, 4, 6, 8, 12-14, 34, 36, 37	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
—	—

AUG 4 1998

RECEIVED IN BOX INTERFERENCE

Instructions

1. For every patent involved in the interference, check if the maintenance fees have been paid by using the patent number with PALM screen 2970. If fees are due and they have not been paid, the interference cannot be declared since it would involve an expired patent (35 USC 135(a); 37 CFR 1.606).
2. For each party, identify the patentable (or patented) and unpatentable (pending) claims which correspond to the count (37 CFR 1.601(f), (n); 1.609(b)(2)).
3. For each party, identify the patentable (or patented) and unpatentable (pending) claims which do not correspond to the count (37 CFR 1.609(b)(3)).
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6. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention as the count (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention from the count (37 CFR 1.609(b)(3).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Zonaire Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The application number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/433098	5/3/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/374540	1/19/95	—	—
PCT	US94/14553	12/28/94	—	—
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):
PATENTABLE CLAIMS: UNPATENTABLE CLAIMS:

The claim(s) of this party which does(do) not correspond to this count is(are):
PATENTABLE CLAIMS: UNPATENTABLE CLAIMS:

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):
PATENTABLE CLAIMS: 16-18, 41-48 UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):
PATENTABLE CLAIMS: — UNPATENTABLE CLAIMS: —

AUG 4 1998

RECEIVED IN BOX INTERFERENCE

Instructions

1. For every patent involved in the interference, check if the fees have been paid by using the **patent number** with the PALM screen CR06.
If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC 135(a); 37 CFR 1.606).
2. For each party, separately identify the patentable and unpatentable claims which correspond to the count. (37 CFR 1.601 (f), 1.601 (n), 1.609(b)(2)).
3. For each party, separately identify the patentable and unpatentable claims which do not correspond to the count (37 CFR 1.609(b)(3)).
4. Forward all files including those the benefit of which is being accorded.
5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate sheet(s) and type-written.

5. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/430784	4/27/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
25, 28-38	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
—	—

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/425020	4/18/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	I-YT
US	08/196689	2/15/94	—	—
US	08/185607	1/21/94	—	AUG 4 1998
US	08/176553	1/4/94	—	

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
35, 38-48, 50, 53-56, 58-67	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
—	—

RECEIVED IN BOX INTERFERENCE

Instructions

1. For every patent involved in the interference, check if the fees have been paid by using the **patent number** with the PALM screen CR06.
   If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC 135(a); 37 CFR 1.606).
2. For each party, separately identify the patentable and unpatentable claims which correspond to the count. (37 CFR 1.601 (f), 1.601 (n), 1.609(b)(2)).
3. For each party, separately identify the patentable and unpatentable claims which do not correspond to the count (37 CFR 1.609(b)(3)).
4. Forward all files including those the benefit of which is being accorded.
5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate sheet(s) and type-written.

5. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Tomaine Thornton	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Eaton	08/434618	5/3/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/374540	1/18/95	—	—
US	08/249376	5/25/94	—	—
US	08/223263	4/4/94	—	—
US	08/185607	1/21/94	—	—
US	08/176553	1/3/94	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 37, 41-50 UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — UNPATENTABLE CLAIMS: —

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Miyazaki	08/592007	1/26/96	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/535025	11/30/95		
US	08/381478	1/31/95		
US	08/361811	12/22/94		
US	08/320300	10/11/94		
US	08/278083	7/20/94		
US	08/221020	4/1/94		
US	08/212164	3/14/94		
JAPAN	6-39090	2/14/94		
JAPAN	6-79842	3/25/94		
JAPAN	6-155126	6/1/94		
JAPAN	6-167328	6/15/94		
JAPAN	6-227159	8/17/94		
JAPAN	6-193169	8/17/94		
JAPAN	6-193916	8/18/94		
JAPAN	6-304167	11/1/94		
JAPAN	6-298669	12/1/94		
JAPAN	6-341200	12/28/94		

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The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 42-61 UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — UNPATENTABLE CLAIMS: —

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary C		

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Miyazaki	08/278083	7/20/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/221020	4/1/94		
US	08/212164	3/14/94		
JAPAN	6-39090	2/14/94		
JAPAN	6-79842	3/25/94		
JAPAN	6-155126	6/1/94		
JAPAN	6-167328	6/15/94		

The claim(s) of this party which correspond(s) to this count is(are):
PATENTABLE CLAIMS 18-37 UNPATENTABLE CLAIMS —

The claim(s) of this party which does(do) not correspond to this count is(are):
PATENTABLE CLAIMS — UNPATENTABLE CLAIMS —

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Miyazaki	08/592027	1/26/96	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/535025	11/30/95		
US	08/381478	1/31/95		
US	08/361811	12/22/94		
US	08/320300	10/11/94		
US	08/278083	7/20/94		
US	08/221020	4/1/94		
US	08/212164	3/14/94		
JAPAN	6-39090	2/14/94		
JAPAN	6-79842	3/25/94		
JAPAN	6-155126	6/1/94		
JAPAN	6-167328	6/15/94		
JAPAN	6-227159	8/17/94		
JAPAN	6-193169	8/17/94		
JAPAN	6-193916	8/18/94		
JAPAN	6-304167	11/1/94		
JAPAN	6-298669	12/1/94		
JAPAN	6-341200	12/28/94		

The claim(s) of this party which correspond(s) to this count is(are):
PATENTABLE CLAIMS 42-49 UNPATENTABLE CLAIMS —

The claim(s) of this party which does(do) not correspond to this count is(are):
PATENTABLE CLAIMS — UNPATENTABLE CLAIMS —

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spencer	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Miyazaki	08/361811	12/22/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/320300	10/11/94		
US	08/278083	7/20/94		
US	08/221020	4/1/94		
US	08/212164	3/14/94		
JAPAN	6-39090	2/14/94		
JAPAN	6-79842	3/25/94		
JAPAN	6-155126	6/1/94		
JAPAN	6-167328	6/15/94		
JAPAN	6-227159	8/17/94		

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY

I-VI

AUG 4 1998

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 43-67

UNPATENTABLE CLAIMS: —

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The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: —

UNPATENTABLE CLAIMS: —

Instructions

1. For every patent involved in the interference, check if the fees have been paid by using the **patent number** with the PALM screen CR06.
If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC 135(a); 37 CFR 1.606).
2. For each party, separately identify the patentable and unpatentable claims which correspond to the count. (37 CFR 1.601 (f), 1.601 (n), 1.609(b)(2)).
3. For each party, separately identify the patentable and unpatentable claims which do not correspond to the count (37 CFR 1.609(b)(3)).
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5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate sheet(s) and type-written.

5. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Rosenberg	08/227530	4/14/94	5,571,686	11/5/96

If application has been patented, have maintenance fees been paid? ___Yes ___No X Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
NONE				

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
1-3	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
4	—

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Kaushansky	08/347748	12/1/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/335566	11/7/94		
US	08/288417	8/9/94		
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
9-13, 15-22, 24-31	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
—	—

Instructions

1. For every patent involved in the interference, check if the fees have been paid by using the **patent number** with the PALM screen CR06.

If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC [illegible] including those the benefit of which is being accorded.

2. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate sheet(s) and type-written.

5. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/19/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary C Lee		

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

PTO-850-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Kaushansky	08/461819	6/6/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/347748	12/1/94		
US	08/335566	11/7/94		
US	08/288417	8/9/94		
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 1-8 UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — UNPATENTABLE CLAIMS: —

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/252491	6/1/94	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/215203	3/21/94		
US	08/203197	2/25/94		AUG 4 1998
US	08/196025	2/14/94		
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The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 10,11,13,20,22-24,27,28,32,33 UNPATENTABLE CLAIMS:

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: UNPATENTABLE CLAIMS:

Instructions

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If fees are due and they have not been paid, the interference cannot be declared since it would invovlve an expired patent. (35 USC 135(a); 37 CFR 1.606).

[illegible] identify the patentable and unpatentable claims which correspond to the count

All information requested below must be attached on (a) separate sheet(s) and type-written.

5. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
12/9/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97	Mary Clem		

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PTO-850-(Rev. 9-27-95)

INTERFERENCE INITIAL MEMORANDUM

Count # 1

BOARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases:

This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/462263	6/5/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 42, 44-50 — UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — — UNPATENTABLE CLAIMS: —

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/463655	6/5/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 42, 46-61 — UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — — UNPATENTABLE CLAIMS: —

AUG 4 1998

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3. For each party, separately identify the patentable and unpatentable claims which do not correspond to the count (37 CFR 1.609(b)(3)).
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12/9/97	Lorraine Spector	308-1793	1812
DATE	GROUP DIRECTOR SIGNATURE (if required)		
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INTERFERENCE INITIAL MEMORANDUM

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This interference involves ____ parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/461072	6/5/95	—	—

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
34, 42-46	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
—	—

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/463956	6/5/95		

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
39, 40, 42-51	—

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS	UNPATENTABLE CLAIMS
—	—

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DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

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PTO-850-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM Count #_____

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PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Holly	08/464984	6/5/95		

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	08/252491	6/1/94		
US	08/215203	3/21/94		
US	08/203197	2/25/94		
US	08/196025	2/14/94		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 36,42-50 UNPATENTABLE CLAIMS: —

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: — UNPATENTABLE CLAIMS: —

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY

If application has been patented, have maintenance fees been paid? ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: UNPATENTABLE CLAIMS:

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: UNPATENTABLE CLAIMS:

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DATE	GROUP DIRECTOR SIGNATURE (if required)		
12/19/97			

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Proposed interference counts for TPO:

1. An isolated, naturally occurring *mpl* ligand or a fragment or derivative thereof which retains the ability to bind the *mpl* receptor, or

an isolated nucleic acid which encodes said *mpl* ligand or fragment or derivative thereof, or

a nucleic acid which hybridizes under moderately stringent conditions to a naturally occurring nucleic acid which encodes said *mpl* ligand or a fragment or derivative thereof, or

a method of stimulating mammalian cell proliferation, differentiation or maturation comprising administering, *in vitro* or *in vivo,* a composition comprising an effective amount of an isolated, naturally occurring *mpl* ligand or a fragment or derivative thereof which retains the ability to bind the *mpl* receptor.

Introduction:

The interference in question centers on the cloning of thrombopoietin (TPO), a protein which has been long sought in the art. The protein was suspected to exist and was sought as far back as 1959. There have been various reports over the years in which groups have attempted to isolated the protein responsible for TPO activity, namely the ability to stimulate hematopoiesis (growth of blood cells in general) and/or thrombopoiesis (growth of thrombocytes, commonly called platelets). One notable report of the purification of thrombopoietin is U.S. Patent number 5,128,449, discussed further below. TPO was cloned in 1994 by several groups, many of which are involved in this interference proceedings. The receptor to the protein was obtained prior to the protein itself. That receptor is known as *mpl* or the *mpl receptor*; hence some parties refer to the protein as *mpl ligand.* It is this functional term that has been used in drafting the proposed interference count. Other names by which mpl ligand is known include thrombopoietin (TPO), megapoietin, and megakaryocyte growth and differentiation factor (MGDF). Some of the claims involved in this interference make specific reference to growth or maturation of cells other than platelets, such as erythrocytes. It is not known at what cellular stage TPO acts, i.e. exactly what platelet progenitor is subject to the biological activity of TPO. However, it is relevant that erythrocytes, platelets, macrophages and neutrophils all descend from myeloid stem cells, and that myeloid stem cells, eosinophils and basophils all descend from pluripotent stem cells. Thus, for example, a cytokine which stimulated the

differentiation of myeloid stem cells would be expected to result in increased production of erythrocytes, platelets, macrophages and neutrophils.

There are 35 individual applications or "parties" involved in this interference. However, as several of the assignees hold more than one involved application, the cases may be grouped by assignee into six groups. The attached spreadsheet lists, by assignee, each case involved in this interference. It is noted that only those cases which have at least one claim in condition for allowance are represented; there are numerous other cases pending at this time which, when allowable subject matter is agreed upon, may be appropriate for inclusion in this proceedings.

Please note that there are numerous Japanese priority documents to which priority is claimed for the Miyazaki applications (assignee, Kirin). The certified translations of these documents are being forwarded in a single, clearly labeled box.

Numerous references have been cited by the Examiner in support of the correspondence of individual claims to the proposed interference count. These are being forwarded to the Board herewith:

United States Patents:

5,264,209	Mikiyama et al.	11/23/93
4,002,531	Royer	1/11/77
4,847,325	Shadle et al.	7/11/89
5,260,417	Grant et al.	11/9/93
5,128,449	McDonald et al.	7/7/92
5,073,627	Curtis et al.	12/17/91
5,441,868	Lin	8/15/95
5,116,964	Capon et al.	5/26/92

Non-Patent Publications:

Pharmacia Biotech. Catalog, 1993, pages 80-81.

F.J. deSauvage et al., "Stimulation of megakaryocytopoiesis and thrombopoiesis by the c-Mpl ligand", Nature 369:533, 1994.

Statements under 37 C.F.R. 1.609(b)(2) and (3): Correspondence of claims to the count:

1. U.S. Patent number 5,593,666

Application Serial Number 08/330517

Inventor: T.P. McDonald

This patent is drawn to compositions comprising thrombopoietin (TPO) and methods of using such compositions. The patent states at column 7, lines 8-10 that the TPO used therein is that of U.S. Patent number 5,128,449 (misprinted in the patent as 5,128,499, which is an unrelated patent) to the same inventor. However, as a source of cloned TPO, the patent refers to admitted prior art by de Sauvage et al. (Nature 369:533-538, 1994) and Lok et al. (Nature 369:565-568, 1994), see column 3 lines 16-17 and 44-45. The claims that are designated as corresponding to the count all encompass within their scope the proteins disclosed by de Sauvage et al. and Lok et al., which proteins are recognized in the art as being the ligand to the *mpl* receptor. Claim 1 corresponds to the count because a C-terminal fragment of TPO sufficient to increase platelet counts is within the metes and bounds of the count, and a method of increasing platelet cell counts falls within the metes and bounds of stimulating mammalian cell proliferation differentiation or maturation. The limitations of dependent claims 2-4 are drawn to the cause of the medical condition being treated, and do not affect the method itself. Dependent claims 5 and 6 introduce limitations as to the dosage and time of administration. Determination of dosage and administration are considered in the art to constitute routine optimization that is the normal purview of the pharmacologist, and therefore the recited limitations are considered to be *prima facie* obvious over the count. Claims 7 and 8 recite the inclusion of other cytokines in the pharmaceutical composition being used in the method of claim 1. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the combination of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious. Independent claim 9 and its dependent claims 10-12 are drawn to a method of increasing platelet cell counts using at least 40 units of mpl ligand, which falls within the metes and bounds of the proposed count. As stated above, optimization of dosage and the particular condition being treated are considered to be *prima facie* obvious over a method of using TPO to stimulate

mammalian cell proliferation, differentiation or maturation. Independent claim 14 is drawn to a composition for use in the method of claim 1 (for example), and differs from the count in reciting a desired outcome, which is not patentably distinct from the count, as it would be reasonably expected to be achieved using the *mpl* ligand. The inclusion of the protein recited in the count in a pharmaceutical composition is considered to be *prima facie* obvious as the person of ordinary skill in the art would immediately understand that the biological activity of TPO has pharmaceutical application. The limitations of claims 15-17 are similar to those of claims 5-8 and are considered obvious for reasons cited above. Claim 18 is also drawn to a composition for the treatment of thrombocytopenia, said composition comprising the mpl ligand; the composition and amounts are considered obvious for reasons cited above. Claim 20 and its dependent claims 21-27 differ from claims 1-7 only in that the full-length species of TPO, specifically excluded from claims 1-7, is included within the metes and bounds of the claims. These claims are considered to correspond to the count for the same reasons as claims 1-7.

Claims 13 and 19 of U.S. Patent number 5,593,666 do not correspond to the proposed count. These claims specifically define the active TPO polypeptide in a manner consistent with the prior McDonald patent, U.S. Patent number 5,128,449. These claims are considered to be patentably distinct from the count because there are substantial differences between the protein as claimed and the protein of the proposed interference count. Specifically, it is noted that the claimed protein is described as having a molecular weight (as determined by SDS-PAGE) of 15,000 daltons (15 kD) as a monomer, and about 30 kD as a dimer. The TPO which is the mpl ligand has not been reported to form a dimer, and has a monomeric molecular weight of approximately 38 kD (estimated), see for example de Sauvage et al. (Nature 369:533) at page 535. Further physical differences between the thrombopoietin of McDonald 5,128,449 have been set forth in the prosecution of other cases involved in this interference, see for example the prosecution history of application serial number 08/223263. In summary, as the protein which has become accepted in the art as being the mpl ligand does not meet the physical limitations set forth in claims 13 and 19, those claims do not correspond to the proposed count.

2. Application Serial Number: 08/252628

Inventor: Bosselman

Allowed claims: 37, 38 and 40-46

The allowed claims, 37, 38 and 40-46, are drawn to DNA encoding human mpl ligand (SEQ ID NO:25 of the application), which is directly encompassed by the proposed count. The patentability of the claims is predicated on the identity of the DNA itself and the protein it encodes; the vectors, host cell and method of producing the encoded protein are obvious over the DNA, as the use of such vectors for recombinant expression of the encoded protein is old and routine in the art.

3. Application Serial Number: 08/481265

Inventor: Bartley

Allowed claims: 84-92

Allowable claim 86 is drawn to an isolated polypeptide having the structure: Met-Lys-residues 1-150 of human mpl ligand-termination at a residue selected from residues 151-244 of human mpl ligand. The claim corresponds to the count because such is a fragment of human mpl ligand which binds to the mpl receptor (such binding being an inherent property of the region included by residues 7-151 of the protein). The claim is allowable over the prior art, but is dependent from claim 85, which is subject to a double-patenting rejection.

Claims 84, 85 and 87-92 are not allowable, being subject to double patenting rejections. These claims correspond to the proposed interference count because they are drawn to a protein which is a functional fragment of human mpl ligand, and pharmaceutical compositions comprising such. The pharmaceutical compositions are considered to be obvious over the protein itself, as it would have been obvious to formulate a composition comprising TPO to be used for its known and expected property of stimulating mammalian cell proliferation, differentiation of maturation.

4. Application Serial Number :08/413802

Inventor: Bartley

Allowed claims: 144-151

Claims 144-151 are drawn to isolated human TPO, including both the mature forms (1-332 of SEQ ID NO: 25) and with the secretory leader sequence attached (-21-332).The pharmaceutical compositions of claims 149-151 are considered to be obvious over the protein itself, as it would have been obvious to formulate a composition comprising TPO to be used for its known and expected property of stimulating mammalian cell proliferation, differentiation of maturation.

5. Application Serial Number: 08/196689

Inventor: Eaton

Allowed claims: 11-13, 16-20, 28-38

Independent claim 11 is drawn to an isolated nucleic acids encoding the protein of SEQ ID NO: 4 of the application, which encodes human mpl ligand. Claim 11 is encompassed by, and therefore corresponds to, the proposed interference count. Claim 12 is drawn to various truncations of the nucleic acid encoding the protein of SEQ ID NO:4, and is similarly encompassed by the proposed interference count, as all recited species encode a protein with mpl binding activity. claim 13 is drawn to a nucleic acid consisting of the open reading frame (coding region) of SEQ ID NO: 5, which encodes the human mpl ligand. Claim 13 is encompassed by, and therefore corresponds to, the proposed interference count.

Dependent claims 16-20 and 28-38 are drawn to vectors and host cells comprising the nucleic acids of the independent claims, as well as the use of said nucleic acids to effect the recombinant expression of the encoded protein. The patentability of the claims is predicated on the identity of the nucleic acid itself and the protein it encodes; the vectors, host cell and method of producing the encoded protein are obvious over the nucleic acid, as the use of such vectors for recombinant expression of the encoded protein is old and routine in the art.

6. Application Serial Number: 08/249376

Inventor: Eaton

Allowed claims: 26-31, 38-46

Independent claim 38 is drawn to an isolated nucleic acid which encodes an *mpl* ligand, encompassing both naturally occurring human mpl ligand and derivatives which retain mpl ligand activity, and thus corresponds to the proposed interference count. Dependent claims 26-31 are drawn to vectors, host cells and expression of the nucleic acid of claim 38. These claims correspond to the count because the patentability of the claims is predicated on the DNA of the independent claim; the dependent claims merely recite elements that are obvious and known in the art (i.e. it is obvious to connect a desired coding sequence to appropriate regulatory sequences and a vector, and to use such to transform host cells and produce the encoded protein). Dependent claims 39, 40, 42-46 specify additional variants within the scope of the independent claim, all of which fall within the metes and bounds of the proposed count.

Claim 41 specifies a nucleic acid which encodes a fusion protein in which the mpl ligand is fused to erythropoietin. Claim 41 is obvious over the proposed interference count in view of Curtis et al. U.S. Patent Number 5,073,627, and Lin, U.S. Patent number 5,441,868.

Curtis et al. teach chimeric proteins in which IL-3 is fused to GM-CSF. The particular proteins were chosen for the fusion because they "have considerable overlap in their broad range of biological activities" (column 1, lines 27-29), specifically that they are both hematopoietic proteins. Curtis et al. do not teach a fusion of IL-3 to thrombopoietin, a.k.a. mpl ligand.

Lin et al. teaches recombinant production of erythropoietin, which is disclosed as being a hematopoietic protein.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand as taught by the proposed interference count and EPO as taught by Lin in the fusion protein of Curtis et al., to obtain a bifunctional hematopoietic protein. The ordinary artisan would have been motivated to do so in view of Curtis' teachings that it is desirable to combine such activities, and would have expected the resultant fusion protein to be at least as effective as the two cytokines administered together as a composition, rather than a fusion protein.

7. Application Serial Number: 08/348658

Inventor: Eaton

Allowed claims: 13, 15, 16

Allowed claims 13, 15 and 16 are drawn to isolated nucleic acids which comprise a specified fragment of the nucleic acid encoding human mpl ligand (SEQ ID NO:4). Although claims 13 and 15 do not specify that the claimed nucleic acid encodes a protein which has mpl ligand activity (i.e. binds to the mpl ligand), the claims nonetheless correspond to the proposed interference count because they encompass, due to the use of the open term "comprising", substantial subject matter within the metes and bounds of the proposed count. This is further evidenced by claim 16, drawn to a cDNA within the metes and bounds of claim 13, which encompasses nucleic acids which include the complete coding region of mpl ligand. (The Examiner notes that a limitation that the claimed molecule is cDNA is essentially a product by process limitation, indicating that the claimed nucleic acid was obtained by the process of isolating mRNA (the type of nucleic acid used *in vivo* for the synthesis of proteins), and using the mRNA as a template to synthesize a DNA molecule complementary to that mRNA, hence the designation "cDNA".)

8. Application Serial Number: 08/422020

Inventor: Eaton

Allowed claims: 20-23, 32-42

Independent claim 32 is drawn to a nucleic acid encoding a human mpl ligand comprising a particular sequence of amino acids, residues 1-153 of SEQ ID NO: 1 of the application. As amino acids 1-153 would be sufficient for binding to the mpl receptor, the claim falls within the metes and bounds of the proposed interference count. Claim 33 requires a nucleic acid encoding the full length of the disclosed mpl ligand, Claim 35 is drawn to various truncations of the nucleic acid encoding the protein of SEQ ID NO:1, and is similarly encompassed by the proposed interference count, as all recited species encode a protein with mpl binding activity.

Claims 34 and 36 specify that the claimed nucleic acid further encodes an amino-terminal methionine residue. Such N-terminal extensions are a common artifact of the cloning process, for example, when expressing a mammalian protein it is common to include an N-terminal methionine,

such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the immunogenic properties of the protein. Therefore, it would have been obvious to the person of ordinary skill in the art to include in the nucleic acid of the proposed interference count a segment encoding an N-terminal methionine.

Dependent claims 20-23 and 37-42 are drawn to vectors, host cells and expression of the nucleic acid of the claims above. These claims correspond to the count because the patentability of the claims is predicated on the DNA of the independent claim; the dependent claims merely recite elements that are obvious and known in the art (i.e. it is obvious to connect a desired coding sequence to appropriate regulatory sequences and a vector, and to use such to transform host cells and produce the encoded protein).

9. Application Serial Number: 08/431378

Inventor: Eaton

Allowed claims: 16-21, 28

The independent claim, claim 28, is drawn to a nucleic acid encoding a human mpl ligand comprising a particular sequence of amino acids, residues 1-153 of SEQ ID NO: 4. As amino acids 1-153 would be sufficient for binding to the mpl receptor, the claim falls within the metes and bounds of the proposed interference count. Dependent claims 16-21 include limitations as to are drawn to vectors, host cells and expression of the nucleic acid of claim 28. These claims correspond to the count because the patentability of the claims is predicated on the DNA of the independent claim; the dependent claims merely recite elements that are obvious and known in the art (i.e. it is obvious to connect a desired coding sequence to appropriate regulatory sequences and a vector, and to use such to transform host cells and produce the encoded protein).

10. Application Serial Number: 08/433103

Inventor: Eaton

Allowed claims: 22-26, 28-33, 40-42

The independent claim, claim 22, is drawn to a nucleic acid encoding a human mpl ligand

comprising a particular sequence of amino acids, residues 7-151 of SEQ ID NO: 1. As amino acids 7-151 would be sufficient for binding to the mpl receptor, the claim falls within the metes and bounds of the proposed interference count. Dependent claims 23-25 are drawn to particular species, all of which also meet the limitations of the proposed count. Independent claim 26 corresponds to the proposed count because it recites a nucleic acid encoding a variant of the human mpl ligand, which is within the scope of the count. Dependent claims 28-33 include limitations as to are drawn to vectors, host cells and expression of the nucleic acid of claim 22. These claims correspond to the count because the patentability of the claims is predicated on the DNA of the independent claim; the dependent claims merely recite elements that are obvious and known in the art (i.e. it is obvious to connect a desired coding sequence to appropriate regulatory sequences and a vector, and to use such to transform host cells and produce the encoded protein).

11. Application Serial Number: 08/223263

Inventor: Eaton

Allowed claims: 1, 4, 7, 9, 28, 30-37, 40

The independent claim, claim 1 is drawn to human mpl ligand or a truncated form of mpl ligand having at least the first 153 amino acid residues; similarly, claim 40 recites specifically an mpl ligand having residues 1-153 of the disclosed sequence. Such a species binds mpl receptor. Thus, claims 1 and 40 fall within the metes and bounds of the proposed interference count, as do dependent claims 4 and 7. With regard to claim 4, human mpl ligand would reasonably be expected to be non-immunogenic in a human. With respect to claim 7, it is noted that mpl ligand produced in a bacterial host cell would not be glycosylated; thus this limitation requires a physical difference between the claimed mpl ligand and the naturally occurring (glycosylated) form; however, the non-glycosylated form would still fall within the metes and bounds of the proposed count. Claim 9 introduces the limitation that the isolated mpl ligand is encoded by a nucleic acid which hybridizes under stringent conditions to that of Figure 8 of the application; such falls within the metes and bounds of being a derivative of mpl ligand which retains the ability to bind the mpl receptor (based upon the recitation that the protein remains an mpl ligand). Claims 28 and 30-37 depend from claim 1. Claim 28

corresponds to the count because it would have been obvious to formulate a pharmaceutical composition comprising the mpl ligand of claim 1 in view of its known and expected properties.

Claims 30 and 31 contain the limitation that the composition of claim 28 comprises other cytokines. These claims are obvious over the proposed interference count in view of U.S. Patent number 5,260,417. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the combination of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious. Claims 32 and 33 recite particular terminal residues for the claimed mpl ligand; as all recited species would be expected to bind mpl receptor, the claims are encompassed by the proposed count. Claims 34 and 36 recite the inclusion of "an N-terminal extension" on the claimed mpl ligand , including the recitation that the protein remains non-immunogenic in a human (claim 36). Such N-terminal extensions are a common artifact of the cloning process, for example, when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the immunogenic properties of the protein. Finally, claims 35 and 37 recite the attachment of the claimed protein to polyethylene glycol (PEG). Such is considered obvious as follows:

Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the recombinantly produced mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

12. Application Serial Number: 08/348657

Inventor: Eaton

Allowed claims: 1, 2, 19

Claim 1 is a naturally occurring porcine (pig) mpl ligand, which is within the metes and bounds of the proposed count. Dependent claim 2 recites biological activity limitations which are inherent to mpl ligand and do not impart separate patentability. The composition of claim 19 is obvious over the proposed count because to suspend a protein in a pharmaceutically acceptable carrier is routine in the art and obvious in view of the known and expected properties of the mpl ligand . It is routine in the art to suspend proteins in physiological buffers, which would meet the limitations of the claim.

13. Application Serial Number: 08/425095

Inventor: Eaton

Allowed claims: 1, 34, 38-40, 44-46

The independent claim, claim 1 is drawn to an mpl ligand having at least the first 153 amino acid residues of SEQ ID NO:1 of the application (human protein); dependent claim 38 limits claim 1 to the full length protein having 332 amino acid residues. Both such species bind mpl receptor. Thus, claims 1 and 38 fall within the metes and bounds of the proposed interference count. Claim 34 corresponds to the count because it would have been obvious to formulate a pharmaceutical composition comprising the mpl ligand of claim 1 in view of its known and expected properties.

Claim 39 depends from claim 1 and limits the claimed protein to that having an additional N-terminal methionine. Such falls within the metes and bounds of the proposed interference count because it would be expected to retain mpl binding activity, and thus is a derivative within the

meaning of the count. Further, such N-terminal extensions are a common artifact of the cloning process, for example, when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the immunogenic properties of the protein. Therefore, it would have been obvious to the person of ordinary skill in the art to include in the protein of the proposed interference count an N-terminal methionine.

Claim 40 specifies that the protein of claim 1 comprises a nonproteinaceous polymer such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the recombinantly produced mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claim 44 specifies a particular variant of mpl ligand, R153A R154A. Such substitutions would not be expected to affect mpl binding activity, as residues 1-153 are known to be sufficient for biological activity. Therefore the variant of claim 44 falls within the metes and bounds of the proposed interference count.

Claims 45 and 46 are obvious over the proposed interference count in view of Capon (U.S.

Patent Number 5,116,964).

Capon teaches fusion proteins comprising immunoglobulin polypeptides fused to "ligand binding partners", which are defined as including hormones and growth factors (see column 2, lines 14-19). At column 4, lines 38-43, Capon states that the immunoglobulin (Ig) fusions of the invention "serve to prolong the in vivo plasma half-life of the ligand binding partner..." and "facilitate its purification by protein A". At column 15, Capon as a preferred embodiment fusion to an IgG1 constant region. Capon does not teach Ig fusions to mpl ligand.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand or an mpl binding portion thereof in the Ig fusion proteins of Capon to obtain the benefits of Ig fusions as disclosed by Capon, specifically increased serum half-life and ease of purification.

14. Application Serial Number: 08/429365

Inventor: Eaton

Allowed claims: 1, 2, 4, 24, 26, 27

Claim 1, to native, full length human mpl ligand, is directly encompassed by the proposed interference count. Dependent claim 2 recites biological activity limitations which are inherent to mpl ligand and do not impart separate patentability. The composition of claim 24 is obvious over the proposed count because to suspend a protein in a pharmaceutically acceptable carrier is routine in the art and obvious in view of the known and expected properties of the mpl ligand . It is routine in the art to suspend proteins in physiological buffers, which would meet the limitations of the claim.

Dependent claims 4 and 7 introduce the limitation that the protein has been deglycosylated (but, in claim 7, retains biological activity). The deglycosylation of proteins is routine in the art, and does not impart patentable distinctness to the product. Such may be done to allow determination of molecular weight, to reduce serum half life, etc.

Claims 26 and 27 contain the limitation that the composition of claim 28 comprises other cytokines. These claims are obvious over the proposed interference count in view of U.S. Patent number 5,260,417. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use

multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the combination of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious.

15. Application Serial Number: 08/430018

Inventor: Eaton

Allowed claims: 1, 3-5, 24, 26-31

Claim 1 is drawn to human mpl ligand of various lengths, all of which would retain mpl binding activity, and thus which fall within the metes and bounds of the proposed interference count. Dependent claim 31 includes a recitation of biological activity, which is inherent to the protein itself. Claim 3 introduces the limitation that the claimed protein has a N-terminal methionine residue. The claim is obvious over the proposed interference count because when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the properties of the protein. Claim 4 introduces the limitation that the protein is unglycosylated. This is obvious over the proposed count because it would have been obvious to the person of ordinary skill in the art at the time the invention was made to recombinantly express mpl ligand in bacterial cells, such being generally recognized in the art as being useful recombinant hosts which allow production of large amounts of a desired protein; expression in a bacterial host would inherently result in the production of an unglycosylated protein, as bacteria in general, and *E. coli*, the most commonly used recombinant host, do not glycosylate proteins. The recitation of claim 5 that the mpl ligand shares at least 90% sequence identity with the mpl ligand of claim 3 is obvious over the count, as such species would fall within the metes and bounds of being "derivatives" which retain the ability to bind the mpl receptor (due to the recitation of *'mpl ligand'*). Claim 24 introduces the limitation that the protein is in a composition further comprising a pharmaceutically acceptable carrier. The composition of claim 24 is obvious over the proposed count because to suspend a protein in a pharmaceutically acceptable carrier is routine in the art and obvious in view of the known and expected properties of the mpl ligand . It

is routine in the art to suspend proteins in physiological buffers, which would meet the limitations of the claim. It would further be obvious to make such a composition sterile, consistent with claim 28, as it is generally known that sterile compositions are more stable (less susceptible to contamination), and that such is generally desirable.

Claims 26 and 27 contain the limitation that the composition of claim 24 comprises other cytokines. These claims are obvious over the proposed interference count in view of U.S. Patent number 5,260,417. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the combination of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious.

Claim 29 includes both truncated forms of the particularly disclosed sequence, and proteins 95% identical to such, with the limitation that the molecule binds and activates human mpl receptor. This subject matter falls within the metes and bounds of the interference count, which encompasses both fragments and derivatives which have the ability to bind mpl receptor. Dependent claim 30 introduces the limitation that the protein is attached to a polymer, such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One

of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

16. Application Serial Number: 08/422194

Inventor: Eaton

Allowed claims: 1, 28, 32-42

Independent claims 1 and 41 are drawn to particular truncated forms of the human mpl ligand, SEQ ID NO:1 in this application. All the recited forms comprise at least residues 1-153 and thus would possess mpl binding activity, and thus fall within the metes and bounds of the proposed interference count. Dependent claim 28 is drawn to the protein of claim 1 and a pharmaceutically acceptable carrier. It is routine in the art to suspend proteins in physiological buffers, which would meet the limitations of the claim. Dependent claims 32-35 recite limitations as to the actual length of the molecule, and fall within the metes and bounds of the proposed count for the same reasons as claim 1. Dependent claims 36-38 introduce the limitation that the protein is either glycosylated (37) or unglycosylated (36, 38). The naturally occurring mpl ligand is a glycosylated protein. Whether of not the recombinantly produced, truncated form of the protein is glycosylated depends upon what type of recombinant host cell is selected for use in production of the protein. For example, a mammalian cell would be expected to produce a glycosylated protein, whereas a bacterial cell would produce an unglycosylated protein. As both types of cell are routinely used in the art for recombinant production of proteins, the proteins of claims 36-38 are considered to be *prima facie* obvious over the proposed interference count, and are in fact encompassed by such, which has no limitation on the basis of glycosylation.

Claims 39-40 introduce the limitation that the protein is attached to a polymer, such as PEG.

Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life

and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claim 42, which depends from claim 41, corresponds to the proposed interference count, as a protein having 95% identity of human mpl ligand and having the property of binding mpl falls within the scope of the proposed interference count.

17. Application Serial Number: 08/423194

Inventor: Eaton

Allowed claims: 1, 2, 6, 17, 38-45

Independent claim 1 is drawn to human mpl ligand which has thrombopoietic activity residues 1-153 or a variant which is at least 90% identical to such. The claim corresponds to the proposed count because thrombopoietic activity is an inherent property of human mpl ligand residues 1-153, and because the variants are likewise encompassed by the language "derivative thereof" as found in the proposed interference count. Claims 2, 6, 17, 38 and 39 recited specific species which also fall within the metes and bounds of the proposed count. Claim 2 additionally recites a chimeric protein comprising mpl ligand fused to another protein (4 species listed). This is considered obvious over the proposed count in view of Curtis et al. U.S. Patent Number 5,073,627, and Lin, U.S. Patent number 5,441,868.

Curtis et al. teach chimeric proteins in which IL-3 is fused to GM-CSF. The particular proteins were chosen for the fusion because they "have considerable overlap in their broad range of biological activities" (column 1, lines 27-29), specifically that they are both hematopoietic proteins. Curtis et al. do not teach a fusion of IL-3 to thrombopoietin, a.k.a. mpl ligand.

Lin et al. teaches recombinant production of erythropoietin, which is disclosed as being a hematopoietic protein.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand as taught by the proposed interference count and optionally EPO as taught by Lin in the fusion protein of Curtis et al., to obtain a bifunctional hematopoietic protein. The ordinary artisan would have been motivated to do so in view of Curtis' teachings that it is desirable to combine such activities, and would have expected the resultant fusion protein to be at least as effective as the two cytokines administered together as a composition, rather than a fusion protein.

Claims 44 and 45, which depend from claim 2, are drawn to variants which have (44) unspecified or (45) specified amino acid substitutions. These variants fall within the metes and bounds of the proposed interference count as being "derivatives". It is routine in the art to make substitutions within a protein for various purposed, such as to introduce or eliminate glycosylation sites, or to eliminate proteolytic cleavage sites. Therefore, in the absence of any unexpected result or property due to such substitutions, such substitutional variants are considered to be *prima facie* obvious.

Claim 41 introduces the limitation that the protein comprises an N-terminal methionine residue. This is considered obvious over the proposed interference count because the person of ordinary skill in the art would have been aware that when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the properties of the protein, and is *prima facie* obvious because the ordinary artisan knows that a methionine residue is needed for the initiation of protein synthesis in a host cell.

Claims 40 and 42 introduce limitations that the protein of the claims from which they depend is glycosylated, or non-glycosylated, respectively. The naturally occurring mpl ligand is a glycosylated protein. Whether of not the recombinantly produced, truncated form of the protein is glycosylated depends upon what type of recombinant host cell is selected for use in production of the protein. For example, a mammalian cell would be expected to produce a glycosylated protein,

whereas a bacterial cell would produce an unglycosylated protein. As both types of cell are routinely used in the art for recombinant production of proteins, the proteins of claims 40-42 are considered to be *prima facie* obvious over the proposed interference count, and are in fact encompassed by such, which has no limitation on the basis of glycosylation.

Claim 43 introduces the further limitation that the protein is covalently linked to a polymer, such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

18. Application Serial Number: 08/425016

Inventor: Eaton

Allowed claims: 1, 2, 4, 6, 8, 12-14, 34, 36, 37

Independent claim 1 is drawn to an isolated human mpl ligand having SEQ ID NO:6, and falls within the metes and bounds of the proposed interference count.

Independent claim 2 is drawn to an mpl ligand fragment, having thrombopoietic activity, comprising the EPO homologous domain of the protein. This is a reference to the N-terminal portion

of the molecule, which inherently has the thrombopoietic activity, which activity requires the ability to bind to the mpl receptor, and thus falls within the metes and bounds of the proposed interference count. Dependent claim 4 specifies that the protein is linked to a nonproteinaceous polymer. Included within the metes and bounds of such, would be a polymer such as PEG. This claim is obvious over the proposed interference count in view of Shadle et al. and Royer. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claim 6 is drawn to a fragment mpl ligand comprising residues from 1 to 153-331 of SEQ ID NO:6, the sequence of human mpl ligand. This claim is encompassed by the proposed interference count because the mpl binding activity resides within the specified portion of the molecule, that is, the region of residues 1-153. Thus all species encompassed by claim 6 are within the metes and bounds of the proposed interference count. Similarly, claims 12 and 13 are drawn to particular species which fall within the definition of being fragments or derivatives of mpl ligand , and which therefore correspond to the proposed interference count. Claim 8 further limits claim 6, specifying that the protein is unglycosylated. This is obvious over the proposed count because it would have been obvious to the person of ordinary skill in the art at the time the invention was made to

recombinantly express mpl ligand in bacterial cells, such being generally recognized in the art as being useful recombinant hosts which allow production of large amounts of a desired protein; expression in a bacterial host would inherently result in the production of an unglycosylated protein, as bacteria in general, and *E. coli*, the most commonly used recombinant host, do not glycosylate proteins.

Claim 14 is drawn to a fusion protein, wherein the mpl ligand is fused to another protein selected from an immunoglobulin or an interleukin. This claim is obvious over the proposed interference count in view of Curtis et al. U.S. Patent Number 5,073,627.

Curtis et al. teach chimeric proteins in which IL-3 is fused to GM-CSF. The particular proteins were chosen for the fusion because they "have considerable overlap in their broad range of biological activities" (column 1, lines 27-29), specifically that they are both hematopoietic proteins. Curtis et al. do not teach a fusion of IL-3 to thrombopoietin, a.k.a. mpl ligand.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand as taught by the proposed interference count in the fusion protein of Curtis et al., to obtain a bifunctional hematopoietic protein. The ordinary artisan would have been motivated to do so in view of Curtis' teachings that it is desirable to combine such activities, and would have expected the resultant fusion protein to be at least as effective as the two cytokines administered together as a composition, rather than a fusion protein.

Claim 34 introduces the limitation that the protein is in a composition with a pharmaceutically acceptable carrier. This is considered to be *prima facie* obvious over the proposed interference count because it is routine in the art to suspend proteins in physiological buffers, which would meet the limitations of the claim.

Claims 36 and 37 are drawn to compositions comprising the mpl ligand and another cytokine, colony stimulating factor or interleukin. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the combination of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious.

19. Application Serial Number: 08/433098

Inventor: Eaton

Allowed claims: 16-18, 41-48

The claims in this application are directed to chimeric proteins comprising all or a portion of the human mpl ligand. The independent claim, claim 16, recites various portions of the mpl ligand that can be included in the chimer, all of which comprise the region of residues 1-153 of the mpl ligand, and all of which therefore inherently have mpl binding activity.

Claims 16 and 48 are obvious over the proposed interference count because they encompass a species in which the claimed protein consists of a methionine residue attached to the amino (N) terminus of mpl ligand or one of the specified fragments thereof. This is considered obvious over the proposed interference count because the person of ordinary skill in the art would have been aware that when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell. An addition such as of a single methionine residue would not be expected to appreciably alter the properties of the protein, and is *prima facie* obvious because the ordinary artisan knows that a methionine residue is needed for the initiation of protein synthesis in a host cell.

Claims 16, 18, 41, 42, 46, 47 and 48 are obvious over the proposed interference count in view of Curtis et al. U.S. Patent Number 5,073,627.

Curtis et al. teach chimeric proteins in which IL-3 is fused to GM-CSF. The particular proteins were chosen for the fusion because they "have considerable overlap in their broad range of biological activities" (column 1, lines 27-29), specifically that they are both hematopoietic proteins. Curtis et al. do not teach a fusion of IL-3 to thrombopoietin, a.k.a. mpl ligand.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand as taught by the proposed interference count in the fusion protein of Curtis et al., to obtain a bifunctional hematopoietic protein. The ordinary artisan would have been motivated to do so in view of Curtis' teachings that it is desirable to combine such activities, and would have expected the resultant fusion protein to be at least as effective as the two cytokines administered together as a composition, rather than a fusion protein.

Claims 16, 17 and 43-47 are obvious over the proposed interference count in view of Capon

(U.S. Patent Number 5,116,964).

Capon teaches fusion proteins comprising immunoglobulin polypeptides fused to "ligand binding partners", which are defined as including hormones and growth factors (see column 2, lines 14-19). At column 4, lines 38-43, Capon states that the immunoglobulin (Ig) fusions of the invention "serve to prolong the in vivo plasma half-life of the ligand binding partner..." and "facilitate its purification by protein A". At column 15, Capon as a preferred embodiment fusion to an IgG1 constant region. Capon does not teach Ig fusions to mpl ligand.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute mpl ligand or an mpl binding portion thereof in the Ig fusion proteins of Capon to obtain the benefits of Ig fusions as disclosed by Capon, specifically increased serum half-life and ease of purification.

20. Application Serial Number: 08/430784

Inventor: Eaton

Allowed claims: 25, 28-38

Claims in this case are drawn to a method of treating a mammal having or at risk of thrombocytopenia using TPO (mpl ligand) or truncated derivatives or variants which retain activity and are at least 90% or 95% identical to the mpl ligand of SEQ ID NO:4, and a pharmaceutical carrier. All of the recited TPO species are within the metes and bounds of the proposed interference count. It is noted that thrombocytopenia is a deficiency of thrombocytes (platelets) and that the claimed method of treatment would inherently result in an increase of platelets via stimulation of proliferation, differentiation and/or maturation of such. Claims 25, 28-31 and 33-37 differ from the proposed count only in the specification that the composition being used comprises a pharmaceutically acceptable carrier (e.g. 25), that the composition is sterile (e.g. 28), and/or the means of administration (e.g.29, 30). These claims are obvious over the proposed interference count because it is old and routine in the art to suspend a pharmacologically active protein in a pharmaceutically acceptable carrier, to sterilize such a composition, and to optimize the route of administration in a method such as that of the proposed interference count. Determination of

dosage and administration are considered in the art to constitute routine optimization that is the normal purview of the pharmacologist, and therefore the recited limitations are considered to be *prima facie* obvious over the count.

Claims 32 and 38 differ from the proposed interference count in that they specify that the mpl ligand further comprises a nonproteinaceous polymer such as PEG. These claims are obvious over the proposed interference count in view of Shadle et al. and Royer. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of using mpl ligand to stimulate cell proliferation by attachment of PEG to the mpl ligand as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

21. Application Serial Number: 08/425020

Inventor: Eaton

Allowed claims: 35, 38-48, 50, 53-56, 58-67

Claims in this case are drawn to a method of treating a mammal having or at risk of thrombocytopenia using TPO (mpl ligand) or truncated derivatives which retain activity. All of the recited TPO species are within the metes and bounds of the proposed interference count. It is noted

that thrombocytopenia is a deficiency of throbocytes (platelets) and that the claimed method of treatment would inherently result in an increase of platelets via stimulation of proliferation, differentiation and/or maturation of such. Thus, claims 35, 38, 39, 47, 53, 58, 60 and 61 are directly encompassed by the proposed interference count. Claim 65, while not encompassed by the proposed interference count, is nonetheless anticipated by such, as numerous of the species of part (a) of the claim (those without the N-terminal methionine) are encompassed by the proposed interference count. Claim 65 additionally encompasses variants which are 95% identical to mpl ligand and which retain biological activity, and which therefore also fall within the metes and bounds of the proposed interference count. Claims 40 and 54 introduce the limitation that the mpl ligand used in the claimed method comprises an additional N-terminal methionine residue, an option that is also recited in claim 65(a). This is considered obvious over the proposed interference count because the person of ordinary skill in the art would have been aware that when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell, and because it would have been obvious to use such recombinantly produced mpl ligand in the method of the proposed interference count, as the person of ordinary skill in the art is generally aware of the desirability of using a recombinantly produced protein, the advantages of such including ease of preparation, and ability to obtain large quantities of a homogeneous product. An addition such as of a single methionine residue would not be expected to appreciably alter the properties of the protein, and is *prima facie* obvious because the ordinary artisan knows that a methionine residue is needed for the initiation of protein synthesis in a host cell.

Claims 41, 55, 64 and 66 introduce the limitation that the mpl ligand used in the claimed method further comprises a non-proteinaceous polymer, such as PEG. These claims are obvious over the proposed interference count in view of Shadle et al. and Royer. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony

stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of using mpl ligand to stimulate cell proliferation by attachment of PEGto the mpl ligand as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claims 42-46, 59 and 67 differ from the proposed count only in the specification that the composition being used is sterile (e.g. 59), and/or the means of administration (42-44) or dosage (45,46, 67). These claims are obvious over the proposed interference count because it is old and routine in the art to sterilize a pharmaceutical composition, and to optimize the route of administration and dosage in a method such as that of the proposed interference count. Determination of dosage and administration are considered in the art to constitute routine optimization that is the normal purview of the pharmacologist, and therefore the recited limitations are considered to be *prima facie* obvious over the count.

Claims 48, 50 and 56 are drawn to a method of treatment comprising administering the mpl ligand and another cytokine, colony stimulating factor or interleukin. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the administration of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious.

Claims 62 and 63 introduce limitations that the protein used in the method of the claims from which they depend is glycosylated, or non-glycosylated, respectively. The naturally occurring mpl ligand is a glycosylated protein. Whether of not the recombinantly produced, truncated form of the protein is glycosylated depends upon what type of recombinant host cell is selected for use in

production of the protein. For example, a mammalian cell would be expected to produce a glycosylated protein, whereas a bacterial cell would produce an unglycosylated protein. As both types of cell are routinely used in the art for recombinant production of proteins and as it would have been obvious to use a recombinantly produced protein in the claimed method, the methods of claims 62 and 63 are considered to be *prima facie* obvious over the proposed interference count, and are in fact encompassed by such, which has no limitation on the basis of glycosylation.

22. Application Serial Number: 08/434618

Inventor: Eaton

Allowed claims: 37, 41-50

Claims in this case are drawn to a method of treating a mammal having or at risk of thrombocytopenia using TPO (mpl ligand) or truncated derivatives which retain activity. All of the recited TPO species are within the metes and bounds of the proposed interference count. It is noted that thrombocytopenia is a deficiency of throbocytes (platelets) and that the claimed method of treatment would inherently result in an increase of platelets via stimulation of proliferation, differentiation and/or maturation of such. Thus, claims 37 and 41-47 correspond to the proposed interference count.

Claims 48-50 - are drawn to a method of treatment comprising administering the mpl ligand and another cytokine, colony stimulating factor or interleukin. The recited cytokines are known in the art to be useful for the stimulation of mammalian cell proliferation, differentiation or maturation. It is further known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7. Therefore, the administration of TPO with other cytokines known in the art to have similar properties is considered *prima facie* obvious.

23. Application Serial Number: 08/592007

Inventor: Miyazaki

Allowed claims: 42-61

Independent claim 42 is drawn to a polynucleotide encoding the human mpl ligand (SEQ ID

NO:6 of the application), which falls within the metes and bounds of the proposed interference count. Independent claim 44 encompasses additional species, all of which fall within the metes and bounds of being variants of mpl ligand; it is noted that species within the metes and bounds of the claim that encode a protein that specifically stimulates or increases platelet production would inherently possess the property of binding to the mpl receptor. The limitations of claim 46 are product by process limitations, that do not materially affect the scope of the claim as it relates to the proposed interference count. Independent claims 48 and 50 introduce the limitation that the encoded protein further has amino terminal met-lys or met residues, respectively, and claim 52 introduces the limitation that a glutathione-S-transferase and thrombin recognition peptide is encoded. These claims are obvious over the proposed interference count because the patentability of the claimed nucleic acids is predicated on the mpl ligand encoding sequence itself, and not the fusion of other sequences to such. For example, Mikayama et al. (U.S. Patent Number 5,264,209) discloses recombinant production of human Interleukin-6 (IL-6), a cytokine with similar biological activity to thrombopoietin. Mikayama discloses at column 5, beginning at line 60, that a preferred variant of the claimed IL-6 has an additional N-terminal methionine, or an N-terminal Met-Lys dipeptide, resulting from the use of a recombinant production method known in the art, in which Cathepsin-C, a diaminopeptidase is used to cleave the Met-Lys dipeptide from the N-terminus of the protein, resulting in the native protein sequence. The production of such a variant is done to allow the use of E. coli as a recombinant host cell. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the nucleic acid of the proposed interference count, to facilitate the use of E. coli as a host cell as disclosed by Mikayama, in view of the art recognized advantages of bacterial host cells, e.g. ability to grow larger cultures faster, resulting in increased production of protein as opposed to that possible with mammalian cells. It therefore would have been obvious to make the DNA constructs encoding Met-Lys-TPO and to use such for the recombinant production of TPO, in view of the disclosure of Mikayama.

With respect to Claim 52, such is obvious over the proposed interference count in view of the Pharmacia Biotech Inc. Molecular and Cell Biology Catalog (1993). The Pharmacia Biotech Inc. Molecular and Cell Biology Catalog (1993), pages 80-81, discloses a set of recombinant vectors, the GST gene fusion system, which are useful for recombinant production of proteins in prokaryotic cells.

Of particular note is that six of the vectors in the right-hand column of page 80 have thrombin cleavage sites 3' of the glutatione-S-transferase-encoding sequences.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to insert the nucleic acid of the proposed interference count into a commercially available vector, such as those sold in the Pharmacia catalog, for the recombinant production of the encoded protein.. The ordinary artisan would have been motivated to use such a vector, as that is the purpose for which the vectors are sold.

Dependent claims 43, 45, 47, 49, 51 and 53-61 are drawn to vectors, host cells and expression of the nucleic acids of the above claims. These claims correspond to the count because the patentability of the claims is predicated on the DNA of the independent claim; the dependent claims merely recite elements that are obvious and known in the art (i.e. it is obvious to connect a desired coding sequence to appropriate regulatory sequences and a vector, and to use such to transform host cells, including CHO cells or *E. coli,* as such are commonly used as recombinant host cells, and produce the encoded protein).

24. Application Serial Number: 08/278083

Inventor: Miyazaki

Allowed claims: 18-37

Independent claim 18 is drawn to a polypeptide which stimulates and increases platelet production, consisting of a continuous amino-terminal fragment of SEQ ID NO: 12 (human mpl ligand) of the application. The scope of the claim is encompassed by the proposed interference count. Claims 20 and 22 are drawn to specific sets of species which also fall within the metes and bounds of the proposed interference count. Independent claim 24 is drawn to an mpl ligand lacking from 1-6 amino terminal residues of the mature protein (it is noted that residues -21 to -1 constitute a secretory signal sequence that would be cleaved and not be found on the mature mpl ligand) as well as one or more C-terminal residues. This claim corresponds to the proposed interference count because such species constitute fragments of the mpl ligand within the metes and bounds of the proposed interference count. Claims 26 and 28 are similar to claim 24, differing in the recitation of particular C-termini; all such species fall within the metes and bounds of the proposed interference

count.

Dependent claims 19, 21, 23, 25, 27 and 29 contain the additional limitation that the claimed protein has an additional amino terminal Methionine residue. This is considered obvious over the proposed interference count because the person of ordinary skill in the art would have been aware that when expressing a mammalian protein it is common to include an N-terminal methionine, such being necessary for the initiation of translation (synthesis of protein) by the recombinant host cell, and because it would have been obvious recombinantly produce mpl, as the person of ordinary skill in the art is generally aware of the desirability of a recombinantly produced protein, the advantages of such including ease of preparation, and ability to obtain large quantities of a homogeneous product. An addition such as of a single methionine residue would not be expected to appreciably alter the properties of the protein, and is *prima facie* obvious because the ordinary artisan knows that a methionine residue is needed for the initiation of protein synthesis in a host cell.

Claim 30 introduces the limitation that the encoded protein further has amino terminal met-lys residues. The claim is obvious over the proposed interference count because the patentability of the claimed protein is predicated on the mpl ligand sequence itself, and not the fusion of other sequences to such. For example, Mikayama et al. (U.S. Patent Number 5,264,209) discloses recombinant production of human Interleukin-6 (IL-6), a cytokine with similar biological activity to thrombopoietin. Mikayama discloses at column 5, beginning at line 60, that a preferred variant of the claimed IL-6 has an additional N-terminal methionine, or an N-terminal Met-Lys dipeptide, resulting from the use of a recombinant production method known in the art, in which Cathepsin-C, a diaminopeptidase is used to cleave the Met-Lys dipeptide from the N-terminus of the protein, resulting in the native protein sequence. The production of such a variant is done to allow the use of E. coli as a recombinant host cell. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the protein of the proposed interference count to comprise additional N-terminal met-lys residues, to facilitate the use of E. coli as a host cell as disclosed by Mikayama, in view of the art recognized advantages of bacterial host cells, e.g. ability to grow larger cultures faster, resulting in increased production of protein as opposed to that possible with mammalian cells.

Claims 31 and 32 introduce the additional limitation that the claimed protein is covalently

bonded to a polymer such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the using mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claim 33 introduces the limitation that the claimed protein is glycosylated. As the naturally occurring mpl ligand is a glycosylated protein, it would have been obvious to make glycosylated mpl ligand. Such glycosylation would be expected to be performed by a mammalian or insect host cell; the use of mammalian or insect cells as hosts for the recombinant production of proteins is old and routine in the art, and is therefore considered to be *prima facie* obvious. Additionally, glycosylated proteins are encompassed by the proposed interference count, which does not contain any limitation as to whether the protein is or is not glycosylated.

25. Application Serial Number: 08/592027

Inventor: Miyazaki

Allowed claims: 42-49

Claim 42 is drawn to full length, mature, mpl ligand having amino acids 1-332 of SEQ ID NO: 6 of the application, which is directly encompassed by the proposed interference count. Claims 43

and 44 contain the limitation that there is an additional N-terminal Met or Gly residue, respectively. and claim 47 additional N-terminal met-lys residues. These variants are encompassed by the proposed interference count. They are also obvious on the basis that additional residues are a common artifact of recombinant production of proteins, and that it would be reasonably expected that the occurrence of such additional residues would not materially affect the properties or activity of the mpl ligand. With further respect to the met-lys combination, the claim is obvious over the proposed interference count because the patentability of the claimed protein is predicated on the mpl ligand sequence itself, and not the fusion of other sequences to such. For example, Mikayama et al. (U.S. Patent Number 5,264,209) discloses recombinant production of human Interleukin-6 (IL-6), a cytokine with similar biological activity to thrombopoietin. Mikayama discloses at column 5, beginning at line 60, that a preferred variant of the claimed IL-6 has an additional N-terminal methionine, or an N-terminal Met-Lys dipeptide, resulting from the use of a recombinant production method known in the art, in which Cathepsin-C, a diaminopeptidase is used to cleave the Met-Lys dipeptide from the N-terminus of the protein, resulting in the native protein sequence. The production of such a variant is done to allow the use of E. coli as a recombinant host cell. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the protein of the proposed interference count to comprise additional N-terminal met-lys residues, to facilitate the use of E. coli as a host cell as disclosed by Mikayama, in view of the art recognized advantages of bacterial host cells, e.g. ability to grow larger cultures faster, resulting in increased production of protein as opposed to that possible with mammalian cells.

Claims 45 and 46 introduce the additional limitation that the claimed protein is covalently bonded to a polymer such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the

general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the using mpl ligand by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

Claims 48 and 49 introduce the limitation that the protein is in a composition with a pharmaceutically acceptable carrier. These claims are obvious over the proposed interference count because it is old and routine in the art to suspend a pharmacologically active protein such as mpl ligand in a pharmaceutically acceptable carrier to be used for its known and expected properties.

26. Application Serial Number: 08/361811

Inventor: Miyazaki

Allowed claims: 43-67

Independent claim 43 is drawn to a method of increasing platelet production using a continuous amino-terminal fragment of SEQ ID NO: 12 (human mpl ligand) of the application. The scope of the claim is encompassed by the proposed interference count.

Claims 46, 49, 52, 55 and 58 are drawn to specific sets of species (various fragments and truncations) which also fall within the metes and bounds of the proposed interference count by virtue of retaining biological activity. Claim 64 contains the limitation that the protein used int he method consists of an additional N-terminal Met residue. This variant is encompassed by the proposed interference count. It is also obvious on the basis that additional residues are a common artifact of recombinant production of proteins, and that it would be reasonably expected that the occurrence of such additional residues would not materially affect the properties or activity of the mpl ligand. Claims 61-63 and 65-67 contain limitations as to the cause of the medical condition being treated; such does not affect the method steps, and therefore falls within the limitations of the proposed

interference count.

Claims 44, 45, 47, 48, 50, 51, 53, 54, 56, 57, 59 and 60 introduce the additional limitation that the protein used in the claimed method is covalently bonded to a polymer such as PEG. Pegylation of proteins (attachment of polyethylene glycol) for the purpose of increasing circulating half life is well known in the art, as evidenced by Royer (U.S. Patent Number 4,002,531) and Shadle et al. (U.S. Patent Number 4,847,325). For example, Royer teaches a method for monopegylation of enzymes to be used as pharmaceuticals, by reductive alkylation.

Shadle et al. disclose the site specific attachment of water soluble polymers to colony stimulating factor-1 (CSF-1). They report that such modification increases the circulating half-life and immunogenicity of the altered protein. At column 2 beginning at line 27, Shadle et al. teach the general desirability of modifying proteins of less than 70 kD to increase their circulating half-life, for example by addition of PEG to the proteins. The paragraph beginning on line 45 of column 4 recites preferred polymers of the invention, which include mPEG, and states specific linkages which may be made to the protein moiety.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of using mpl ligand to comprise using an mpl ligand modified by attachment of PEG as taught by Royer and Shadle et al. One of ordinary skill in the art would have been motivated to do so to attain the known and expected advantages of pegylation, including increased serum half-life of the resulting modified protein.

27. Application Serial Number: 08/227530

Inventor: Rosenberg

Patented claims: 1-4

The claims are drawn to a method "for prolonging survival and viability" of a platelet containing preparation, using megapoietin, which is also known as thrombopoietin, or mpl ligand. The equivalence of the proteins can be inferred from the disclosure that the protein has a molecular weight of 31 kD (col. 4, line 31), that the protein can be isolated from the plasma of thrombocytopenic animals (col. 4) and the disclosed biological activities, see for example columns

6-7. Claim 1 is anticipated by the proposed interference count due to the recitation that the megapoietin being used in the method stimulates an increase in megakaryocyte number and ploidy, which correspond to stimulating mammalian cell proliferation differentiation and maturation as recited in the proposed interference count. The limitations of claim 2 relate solely to the assay for the end result, and fall within the metes and bounds of the proposed interference count. Claim 3 recites that the preparation being treated is whole blood. This is obvious over the proposed interference count because treatment of whole blood reads on *in vivo* administration of mpl ligand, as evidenced by claim 1, and because it would have been obvious to administer megapoietin/mpl ligand to a patient in view of its known and expected properties.

Claim 4 does not correspond to the proposed interference count because it would not have been obvious from the prior art nor the proposed interference count that megapoietin/ mpl ligand would have the effect of prolonging the viability and survival of isolated platelets. Although it was known and expected that mpl ligand would stimulate proliferation, differentiation and/or maturation of various hematopoietic cells, platelets are terminally differentiated cells which do not further differentiation, mature, or proliferate.

28. Application Serial Number: 08/347748

Inventor: Kaushansky

Allowed claims: 9-13, 15-22, 14-31

Independent claim 9 is drawn to a method of stimulating erythropoiesis (red blood cell growth) by administration of a mammalian TPO (mpl ligand) of at least 323 residues of SEQ ID NO: 4 of the application or species homologs thereof. As erythropoiesis falls within the metes and bounds of mammalian cell proliferation, differentiation or maturation, the scope of the claim is encompassed by the proposed interference count.

Independent claim 18 is similar to claim 15, with the additional limitation that the mpl ligand is coadministered with erythropoietin (EPO). It is known in the art to use multiple such cytokines together, see for example U.S. Patent number 5,260,417, claim 7 or column 11, lines 58-60. Therefore, a method of treatment using the combination of TPO with EPO is considered *prima facie* obvious over the proposed interference count. Similarly, dependent claim 24, which specifies that

the EPO is human EPO is obvious as for claim 18, and because it is clear that treatment of humans is contemplated by both the proposed interference count (which encompasses any mammal), and the '417 patent.

The limitations of dependent claims 10-13 and 19-22, are drawn to the cause of the medical condition being treated or diagnostic criteria, and do not affect the method itself. These claims therefore correspond to the proposed interference count.

Dependent claims 15 and 25 have limitations as to the particular species of mpl ligand being used in the claimed method, all of which species are within the metes and bounds of the proposed interference count.

Dependent claims 16, 17 have limitations as to dosage. Determination of dosage and administration are considered in the art to constitute routine optimization that is the normal purview of the pharmacologist, and therefore the recited limitations are considered to be *prima facie* obvious over the count. Claims 28-31 recite specific limitations as to outcome, which limitations to not render the claimed methods patentably distinct from the proposed interference count, as *in vivo* administration of mpl ligand within the scope of the proposed interference count, and with routine dosage optimization as found obvious for claims 16 and 17 would reasonably be expected to lead to a result consistent with the claims.

29. Application Serial Number: 08/461819

Inventor: Kaushansky

Allowed claims: 1-8

Independent claim 1 is drawn to a method of stimulating erythropoiesis (red blood cell growth) *in vitro* using a mammalian TPO (mpl ligand) of at least 323 residues of SEQ ID NO: 4 of the application or species homologs thereof to stimulate bone marrow or peripheral blood cells. As erythropoiesis falls within the metes and bounds of mammalian cell proliferation, differentiation or maturation, the scope of the claim is encompassed by the proposed interference count. Claims 4, 5 and 8 have limitations as to the particular species of mpl ligand being used in the claimed method, all of which species are within the metes and bounds of the proposed interference count. With further

respect to claim 5, culture of bone marrow or peripheral blood cells with TPO within the metes and bounds of the proposed interference count would inherently result in an increase in erythrocyte precursors, therefore a limitation to such does not render the claim patentably distinct from the proposed interference count.

Dependent claims 3 and 7, which limit the TPO to mouse or human, are similarly encompassed by the proposed interference count.

Dependent claims 2 and 6 have limitations as to dosage. Determination of dosage and administration are considered in the art to constitute routine optimization that is the normal purview of the pharmacologist, and therefore the recited limitations are considered to be *prima facie* obvious over the count. Claims 28-31 recite specific limitations as to outcome, which limitations to not render the claimed methods patentably distinct from the proposed interference count, as *in vivo* administration of mpl ligand within the scope of the proposed interference count, and with routine dosage optimization as found obvious for claims 16 and 17 would reasonably be expected to lead to a result consistent with the claims.

30. Application Serial Number: 08/252491

Inventor: Holly

Allowed claims:10, 11, 13, 20, 22-24, 27, 28, 32, 33

Independent claim 1 is drawn to a polynucleotide (nucleic acid) which encodes a naturally occurring mammalian thrombopoietin, and which falls within the metes and bounds of the proposed interference count. Dependent claims 11 and 13 have specific limitations as to the amino acid sequence encoded by, or the nucleic acid sequence itself, and similarly correspond to the proposed interference count by virtue of encoding thrombopoietin, or mpl ligand.

Claim 20 differs from claim 1 in reciting that the claimed nucleic acid is contained in an expression vector. Claim 22, which depends from claim 20, specifies a particular nucleic acid sequence. Claim 23 contains additional limitations as to the vector, and claims 24, 27, 28, 32 and 33 are drawn to host cells and expression of the encoded mpl ligand. These claims all correspond to the proposed interference count because the nucleic acid in question encodes an mpl ligand as

specified in the proposed interference count. The patentability of the claims is predicated on the identity of the DNA itself and the protein it encodes; the vectors, host cell and method of producing the encoded protein are obvious over the DNA, as the use of such vectors for recombinant expression of the encoded protein is old and routine in the art.

31. Application Serial Number: 08/462263

Inventor: Holly

Allowed claims: 42, 44-50

Independent claim 42 is drawn to a plasmid comprising a DNA segment which encodes a naturally occurring mammalian thrombopoietin, and which falls within the metes and bounds of the proposed interference count. Dependent claims 44-48 are drawn to cells transformed with the vector of claim 42. These claims all correspond to the proposed interference count because the nucleic acid in question encodes an mpl ligand as specified in the proposed interference count. The patentability of the claims is predicated on the identity of the DNA itself and the protein it encodes; the vectors, and host cells are obvious over the DNA, as the use of such vectors and host cells for recombinant expression of the encoded protein is old and routine in the art. The limitation of claim 49 that the encoded protein comprises an amino-terminal serine residues is consistent with naturally occurring mpl ligand (the human and murine thrombopoietins both have a serine residue at the amino terminus of the mature protein), and therefore corresponds with the proposed interference count. Similarly, the molecular weight limitation of claim 50 is consistent with the proposed interference count, as the native protein has a molecular weight in the vicinity of 30 kD (and numerous fragments of lesser size retain activity and also fall within the metes and bounds of the proposed interference count).

32. Application Serial Number: 08/463655

Inventor: Holly

Allowed claims: 42, 46-61

Independent claim 42 is drawn to an isolated polynucleotide (nucleic acid) encoding a TPO having from 162-187 amino acids, with at least 80% identity to a region of SEQ ID NO: 2 of the application. This claim corresponds to the proposed interference count because the claimed nucleic acid encodes a functional fragment of mpl ligand. Dependent claims 46-49 contain limitations as to the actual sequence of the claimed DNA, which sequences also fall within the metes and bounds of the proposed interference count. The limitation of claim 50, that the nucleic acid is DNA, corresponds to the count because DNA is a nucleic acid.

Dependent claims 51-61 are drawn to expression vectors and transformed cells comprising a nucleic acid defined as for claim 42, as well as a method for recombinant production of the encoded TPO. These claims all correspond to the proposed interference count because the nucleic acid in question encodes an mpl ligand as specified in the proposed interference count. The patentability of the claims is predicated on the identity of the DNA itself and the protein it encodes; the vectors, host cell and method of producing the encoded protein are obvious over the DNA, as the use of such vectors for recombinant expression of the encoded protein is old and routine in the art.

33. Application Serial Number: 08/461072

Inventor: Holly

Allowed claims: 34, 42-46

Independent claim 34 is drawn to a pharmaceutical composition comprising a TPO (mpl ligand) within the metes and bounds of the proposed interference count. The claim corresponds with the proposed interference count because the pharmaceutical composition is considered to be obvious over the protein itself, as it would have been obvious to formulate a composition comprising TPO to be used for its known and expected property of stimulating mammalian cell proliferation, differentiation of maturation.

Independent claim 42 is drawn to the isolated mpl ligand itself, defining such by biological activity and similarity to SEQ ID NO: 2 of the application, and therefore corresponds to the proposed interference count. Dependent claims 43 and 44 are drawn to particularly disclosed amino acid sequences, for mouse and human TPO respectively, which also fall within the metes and bounds of the proposed interference count. Dependent claims 45 and 46 are drawn to pharmaceutical

compositions comprising specific mpl ligands, which also fall within the metes and bounds of the proposed interference count. The claims correspond with the proposed interference count because the pharmaceutical composition is considered to be obvious over the protein itself, as it would have been obvious to formulate a composition comprising TPO to be used for its known and expected property of stimulating mammalian cell proliferation, differentiation of maturation.

34. Application Serial Number: 08/463956

Inventor: Holly

Allowed claims: 39, 40, 42-51

Independent claim 39 is drawn to a method of stimulating cell proliferation *in vitro* using a mpl ligand of SEQ ID NO: 2 of the application or species homologs thereof to stimulate bone marrow or peripheral blood cells. The scope of the claim is encompassed by and therefore corresponds to the proposed interference count. Independent claim 44 is similar to claim 39 but defines the protein being used in the claimed method differently; however, the protein is still an mpl ligand, and falls within the metes and bounds of the proposed interference count. The limitation of claims 40 and 45 as to the cell type also fall within the metes and bounds of the proposed interference count, the recited cells meeting the limitation of being mammalian cells.

Claims 42, 43, and 46-51 have limitations as to the particular species of mpl ligand being used in the claimed method, all of which species are within the metes and bounds of the proposed interference count.

35. Application Serial Number: 08/464984

Inventor: Holly

Allowed claims: 36, 42-50

Independent claim 36 is drawn to a method of stimulating platelet production in a mammal (*in vivo*) using a mpl ligand of SEQ ID NO: 2 of the application or species homologs thereof. The scope of the claim is encompassed by and therefore corresponds to the proposed interference count. Independent claim 44 is similar to claim 36 but defines the protein being used in the claimed method

differently; however, the protein is still an mpl ligand, and falls within the metes and bounds of the proposed interference count.

Claims 42, 43, and 45-50 have limitations as to the particular species of mpl ligand being used in the claimed method, all of which species are within the metes and bounds of the proposed interference count.

Respectfully submitted,

Lorraine Spector

Lorraine Spector
Patent Examiner

12/19/97

Summary of cases involved in Mpl ligand interference:

1. Assignee: U. Tenn.
Nucleic Acid Cases: None.
Composition, method of treatment:

Assignee	Serial No.	First Inventor	Filing Date	Eff. F.D.	STATUS	Stat. Date	What is claimed?
U. Tenn.	5,593,666	McDonald	10/27/94	10/27/94	PATENT		"C-term. frags." +/- other cytokines compositions, method of use

2. Assignee: Amgen

Nucleic Acid Cases:

Amgen	08/252628	Bosselman	5/31/94	5/31/94	SUSP	2/19/97	Hum. full length, vector, cells, exp'n

Protein Cases:

Amgen	08/413802	Bartley	3/30/95	11/30/94	SUSP	12/97	Full length human, pharm. comp.
Amgen	08/481265	Bartley	8/24/95	PCT 3/30/95,prob. priority claim to 3/31/94 (08/ 221768, LOST)	2F **1 Allowable claim**	10/97	-21-(151-244), 1-(151-244) ± met-lys, pharm comp.

Method of treatment Cases:None.

3. Assignee: Genentech

Nucleic Acid Cases:

Genentech	08/196689	Eaton	2/15/94	2/15/94	SUSP	3/15/96	Human full length, 153+, vector, cells, exp'n
Genentech	08/249376	Eaton	5/25/94	5/25/94	SUSP	5/6/97	Pig, Human full length, 153+, vector, cells, exp'n R153A R154A
Genentech	08/348658	Eaton	12/2/94	12/2/94	SUSP	5/14/97	Human-mature, vector, exp'n
Genentech	08/422020	Eaton	4/13/95	4/4/94	SUSP	12/27/96	Hum. 1-153+, vector, cells, exp'n, N-met
Genentech	08/431378	Eaton	4/27/95	2/15/94	SUSP	12/27/96	Hum 1-153+, vector, cells, exp'n
Genentech	08/433103	Eaton	5/3/95	1/18/95	SUSP	3/24/97	Hum. Comprising 7-151, R153A R154A, encodes 90 or 95% ID, vector, cells, exp'n

Protein Cases:

Genentech	08/223263	Eaton	4/4/94	4/4/94	SUSP	9/30/96	1-(153-332)Human or encoded by hyb. to 1-153, pharm comp. other agents and PEG'd
Genentech	08/348657	Eaton	12/2/94	1/3/94	SUSP	10/22/96	Porcine mpl ligand + Pharm. Comps.
Genentech	08/425095	Eaton	4/18/95	5/25/94	SUSP	12/27/96	1-153(human), 1-332, N-met, polymer, **R153A R154A**, Ig fusion
Genentech	08/429365	Eaton	4/26/95	1/21/94	SUSP	12/27/96	Native full-length human, comp w/ other cytokines
Genentech	08/430018	Eaton	4/27/95	2/15/94	SUSP	1/3/97	Human, spp. of truncates: 153, 164, 191, 205, 207, 217, 229, 245, 332. N-met, Pharm. comp., combo.
Genentech	08/422194	Eaton	4/13/95	4/4/94	SUSP	1/13/97	1-153+, ±glycos., polymer, 95% ID
Genentech	08/423194	Eaton	4/18/95	5/25/94	SUSP	4/7/97	1-153 or 90% ID, truncates, chimers-IgG, IL3, G-CSF, EPO; Glycos., N-met, polymer, variant **R153A R154A**

Genentech	08/425016	Eaton	4/18/95	4/18/95	SUSP	5/6/97	Human, polymer, truncates, 153+, Chimer, **153/154**, fusion, combo.
Genentech	08/433098	Eaton	5/3/95	1/18/95	SUSP	11/6/97	TPO fusion proteins

Method of treatment Cases:

Genentech	08/430784	Eaton	4/27/95	2/15/94	SUSP	2/26/97	treat mammal, ± other cytokines
Genentech	08/425020	Eaton	4/18/95	5/25/94	SUSP	4/97	treat mammal, full length, truncated, polymers
Genentech	08/434618	Eaton	5/3/95	1/18/95	SUSP	9/15/97	in vivo 1-153+, ± polymer, other cytokines

4. Assignee: Kirin

Nucleic Acid Cases:

Kirin	08/592007	Miyazaki	1/26/96	1/2/96	SUSP	11/19/97	1-332 Hum., vector, metlys, met, thrombin recognit'n peptide, cells, exp'n, cleave w/thrombin

Protein Cases:

Kirin	08/278083	Miyazaki	7/20/94	7/20/94	SUSP	12/30/96	N-term. frag, **lacks** at least 232+; N-met, -met-lys, 151+, 163, polymer, pharm. comp.
Kirin	08/592027	Miyazaki	1/26/96	1/2/96	SUSP	10/28/97	full length

Method of treatment Cases:

Kirin	08/361811	Miyazaki	12/22/94		SUSP	11/14/97	Human, murine: in vivo platelet production

5. Assignee: MIT

Nucleic Acid Cases:None
Protein Cases:None
Method of treatment Cases:

MIT	5,571,686	Rosenberg	4/14/94	4/14/94	**PATENT**	11/5/96	prolong Survival & viability of platelet prep., in vitro or vivo

6. Assignee: Zymogenetics
Nucleic Acid Cases:

1 Zymogenetics	08/252491	Holly	6/1/94	6/1/94	SUSP	~3/1/96	Nat. occ. Mamm., vector, cells, exp'n
1 Zymogenetics	08/462263	Holly	6/5/95	6/1/94	SUSP	4/4/97	Mamm., plasmid, cells
1 Zymogenetics	08/463655	Holly	6/5/95	6/1/94	SUSP	6/12/97	encodes 162-187aa, activity, 80% ID to seq., vector, cells, exp'n

Protein Cases:

Zymogenetics	08/461072	Holly	6/5/95	6/1/94	SUSP	4/4/97	Murine, Human, 162-187, 80% ID.

Method of treatment Cases:

Zymogenetics	08/347748	Kaushansky	12/1/94	2/14/94	**ALL** **pulled from issue**		in vivo erythropoiesis-give tpo
Zymogenetics	08/461819	Kaushansky			**ALL** **pulled from issue**		in vitro erythropoiesis-give tpo to bone marrow or periph. blood cells, isolate
Zymogenetics	08/463956	Holly	6/5/95	6/1/94	SUSP	7/29/97	Stem cell prolif. in vitro
Zymogenetics	08/464984	Holly	6/5/95	6/1/94	SUSP	7/28/97	Platelet production in vitro